REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

The limitation of claim 2, i.e. "at least one compound selected from the group consisting of monoethanolamine or its pharmacologically acceptable salt, N-methylglucamine or its pharmacologically acceptable salt, and nicotinamide" is incorporated into claim 1. To clarify the compositions of an aqueous solution preparation of the present invention, the aminoglycoside antibiotic or its pharmacologically acceptable salt is referred to as (a), bromfenac or its pharmacologically acceptable salt is referred to as (b), and monoethanolamine etc. is referred to as (c) in amended claim 1.

Present claims 2 and 5 are deleted.

Claim 4 is amended to refer to the ingredient as (d).

New claim 9 is added. Basis of this amendment is page 9, lines 9-10 and lines 17-19 of the specification.

Turning to the Official Action, the document JP 2683676 corresponds to USP 4,910,225 which was considered. Thus, Applicants think that it is not necessary to have JP 2683676 considered by the Examiner.

There is a single ground of rejection. Claims 1-8 are rejected under 35 USC 103 as unpatentable over Fu et al. (USP 5,414,011) in view of Cagle et al. (USP 6,440,964). This ground of rejection is respectfully traversed as applied to the amended claims.

The claimed invention in amended claim 1 is as follows:

Claim 1: An aqueous solution preparation comprising (a) an aminoglycoside antibiotic or its pharmacologically acceptable salt, (b) bromfenac or its pharmacologically acceptable salt and (c) at least one compound selected from the group consisting of monoethanolamine or its pharmacologically acceptable salt, N-methylglucamine or its pharmacologically acceptable salt, and nicotinamide.

By using (c) in combination with (a) and (b), a stable and clear aqueous solution preparation wherein no precipitation occurs can be obtained.

Fu et al., (USP 5,414,011)

Fu et al. disclose an ophthalmologically acceptable ketorolac formulation. The purpose of Fu et al. is to provide a stable and clear formulation for ketorolac and quaternary ammonium compounds. As described in Fu et al., NSAIDs such as ketorolac have proven to be incompatible with quaternary ammonium compounds because they can form a complex with NSAIDs, rendering the preservative less available to serve its function (for example, see column 1, lines 51-53 and column 2, lines 48-53).

Fu et al. solve the problem, using octoxynol 40, a nonionic polyoxyethylated octylphenol surfactant, which is added to the formulation containing ketorolac and quaternary ammonium compounds. Further, tobramycin is added to the formulation to reduce/prevent the bacterial infection. See column 2, line 66 to column 3, line 4.

On the other hand, the subject matter of the present invention is distinctly different from that of Fu et al.

Until the present invention, with respect to a combined aqueous solution preparation comprising bromfenac and an aminoglycoside antibiotic, stable combined preparations had not yet been known, due to the difficulty in formulation of the above aminoglycoside antibiotic with the non-steroidal anti-inflammatory agent. For example, when tobramycin is combined with diclofenac sodium (which is a non-steroidal anti-inflammatory agent), there is a problem that precipitation or suspension formation occurs, making it difficult to prepare an aqueous solution preparation comprising an aminoglycoside antibiotic and a nonsteroidal anti-inflammatory agent (see page 2, line 29 to page 3, line 7 of the present specification).

In the present invention, a stable aqueous solution containing an aminoglycoside antibiotic and bromfenac wherein no precipitation occurs is provided by adding component (c) of claim 1, i.e. at least one compound selected from the group consisting of monoethanolamine or its pharmacologically acceptable salt, N-methylglucamine or its pharmacologically acceptable salt, and nicotinamide to the solution.

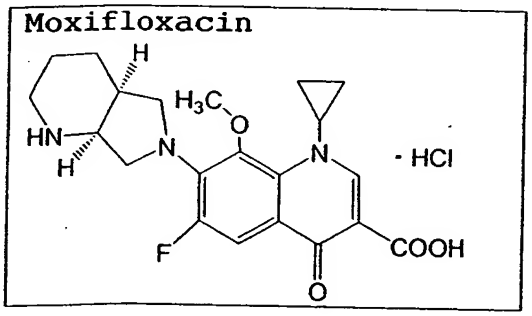
Fu et al. fail to disclose or suggest that the aqueous solution preparation comprising (c) recited in claim 1. Further, Fu et al. neither disclose nor suggest the combination of (a), (b) and (c) recited in claim 1. Nor does Fu et al. disclose or suggest that an aqueous solution preparation containing an aminoglycoside antibiotic and bromfenac does not cause precipitation by containing (c).

Cagle et al. (USP 6,440,964)

Cagle et al. disclose ophthalmic, otic and nasal compositions containing a new class of antibiotics such as Moxifloxacin. Cagle et al. also disclose that the compositions may contain an anti-inflammatory agent such as bromfenac.

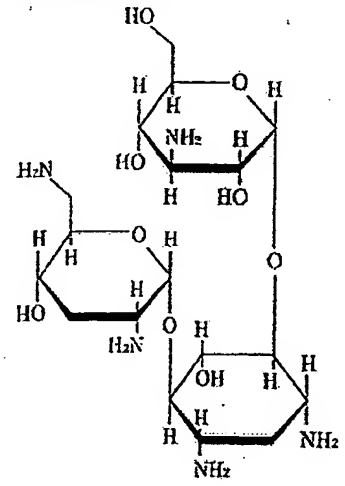
However, the antibiotics used in Cagle et al. are quinolone carboxylic acids. Cagle et al. neither disclose nor suggest that aminoglycoside antibiotics used in the present invention may be used in the composition of Cagle et al. The structure of quinolone carboxylic acids disclosed in Cagle et al. is quite different from that of aminoglycoside antibiotic used in the present invention. For example, the structure of Moxifloxacin disclosed in Cagle et al. as follows:

Moxifloxacin

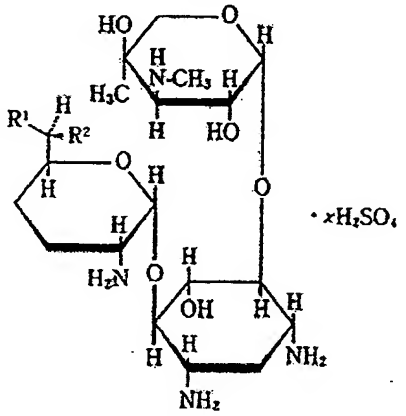


On the other hand, the structures of the major compounds of aminoglycoside antibiotics used in the present invention are as follows:

Tobramycin

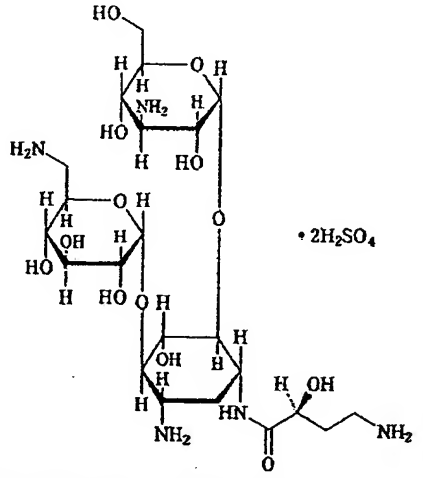


Gentamicin sulfate

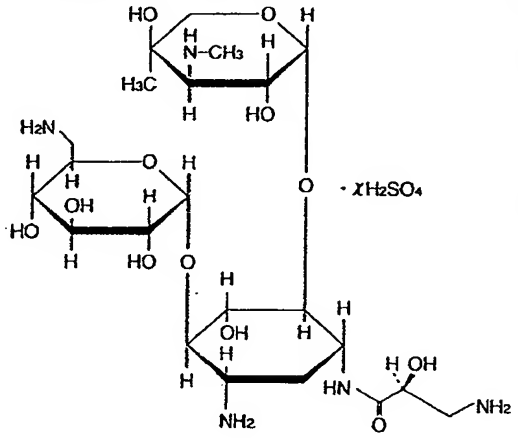


Gentamicin sulfate C_1 : $R^1=CH_3$, $R^2=NHCH_3$
Gentamicin sulfate C_2 : $R^1=CH_3$, $R^2=NH_2$
Gentamicin sulfate C_{1a} : $R^1=H$, $R^2=NH_2$

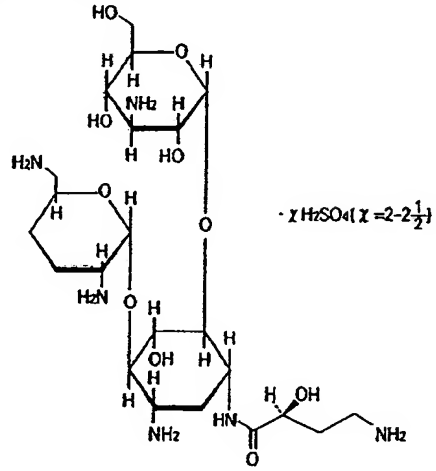
Amikacin sulfate



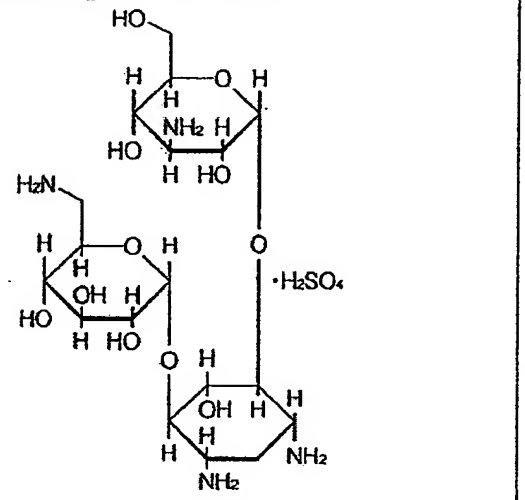
Isepamicin sulfate



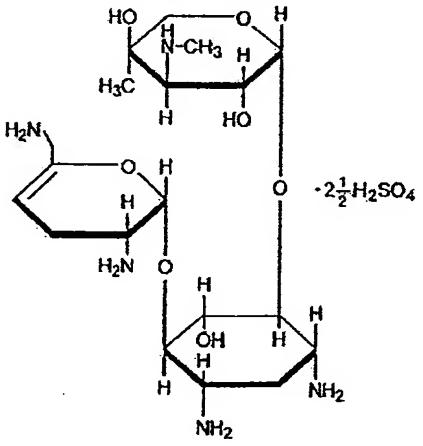
Arbekacin sulfate



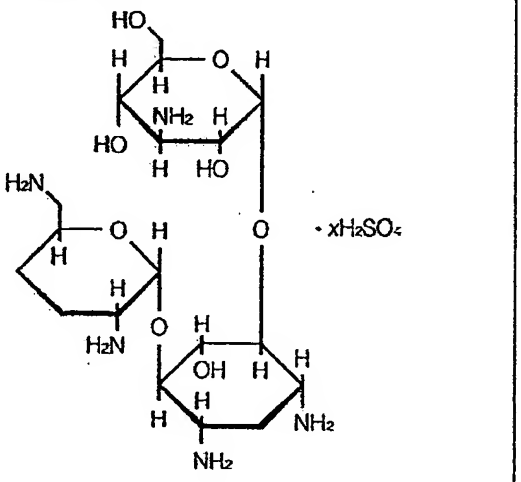
Kanamycin sulfate



Sisomicin sulfate



Dibekacin Sulfate



It is clear from these structural formulas that the antibiotic used in Cagle et al. is quite different from that of the present invention. Accordingly, even if Cagle et al. disclose that bromfenac is one of preferred non-steroidal anti-inflammatory agents in the composition of Cagle et al., a person skilled in the art would not select bromfenac to combine with aminoglycoside antibiotics.

Further, it is neither disclosed nor suggested in Cagle et al. to prepare an aqueous solution preparation comprising (c) recited in claim 1. In addition, Cagle et al. neither disclose nor suggest the combination of (a), (b) and (c) recited in proposed claim 1 and that an aqueous solution preparation containing an aminoglycoside antibiotic and bromfenac does not cause precipitation by containing (c).

Therefore, those skilled in the art would not select and combine (a) an aminoglycoside antibiotic, (b) bromfenac and (c) monoethanolamine etc. from the disclosures of Fu et al. and Cagle et al. Accordingly, the claimed invention is not obvious to those skilled in the art from the cited prior art references.

In summary, there is no teaching or suggestion in the references to prepare the claimed preparation containing (a) an aminoglyoside antibiotic and (b) bromfenac in combination with (c) at least one compound selected from the group consisting of monoethanolamine or its pharmacologically acceptable salt, N-methylglucamine or its pharmacologically acceptable salt, and nicotinamide.

In view of the foregoing, it is believed that each ground of rejection set forth in the Official Action has been overcome, and that the application is now in condition.

Accordingly, such allowance is solicited.

Respectfully submitted,

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